

CLAIMS

1. A method for preparing a grafted homodetic cyclopeptide forming a framework that defines two faces, a so-called upper face and a so-called lower face, said two faces both being grafted,

wherein a linear peptide is synthesized, said synthesis being performed from modified or unmodified amino acids, some of which carry orthogonal protective groups; an intramolecular cyclization of the resulting protected linear peptide is performed; some or all of the orthogonal protective groups are substituted with a protected precursor; at least one molecule of interest is grafted onto one and/or the other face of said framework via an oxime bond.

2. The method for preparing a grafted homodetic cyclopeptide as defined in Claim 1, wherein said synthesis of the linear peptide, performed on the solid phase, is initiated from a glycine residue whose carboxyl function is anchored to a resin, and cyclization of the resulting linear peptide is performed in solution after release of the resin.

3. The method for preparing a grafted homodetic cyclopeptide as defined in Claim 1, wherein said synthesis of the linear peptide and then cyclization thereof are performed entirely on the solid phase.

4. The method for preparing a grafted homodetic cyclopeptide as defined in Claim 3, wherein said synthesis of the linear peptide is initiated with an amino acid residue whose side chain is anchored to a resin.

5. The method for preparing a grafted homodetic cyclopeptide as defined in any of Claims 1 through 4, wherein it is entirely or partially automated on a peptide-synthesizing robot.

6. The method for preparing a grafted homodetic cyclopeptide as defined in any of Claims 1 through 5, wherein said cyclopeptide is constituted from 5, 10, or 14 amino acid residues, preferably 10 amino acids forming a cyclodecapeptide.

7. The method for preparing a grafted homodetic cyclopeptide as defined in Claim 5, wherein the cyclopeptide exhibits 10 or 14 amino acid residues and forms two turns, said two turns being constituted by an (L)Pro-(D)AA and/or (D)Pro-(L)AA combination, AA being an amino acid and preferably glycine, the two turns being separated by three or five amino acid residues, respectively.

8. The method for preparing a grafted homodetic cyclopeptide as defined in either of Claims 6 or 7, wherein said three or five amino acid residues each have, on their side chain, a chemical function initially protected orthogonally by a protective group, the protective groups of the side chains of these amino acids being directed alternately to one side and the other of the median plane of said framework, and defining a so-called lower and upper face with respect to that plane.

9. The method for preparing a grafted homodetic cyclopeptide as defined in any of Claims 6 through 8, wherein said three or five amino acid residues are preferably amino acid residues having an amine side chain, and very preferably lysine.

10. The method for preparing a grafted homodetic cyclopeptide as defined in any of Claims 6 through 9, wherein the orthogonal protective groups of said central amino acid residues are identical to one another, the orthogonal protective groups of said other amino acid residues are identical to one another, the orthogonal protective groups of said central amino acid residues, on the one hand, and the orthogonal protective groups of said other amino acid residues, on the other hand, are different from one another.

11. The method for preparing a grafted homodetic cyclopeptide as defined in Claim 1, wherein grafting of the framework is begun by substituting the orthogonal protective groups of the framework with a protected precursor of the oxyamine function or a protected masked precursor of the aldehyde function, or with a label.

12. The method for preparing a grafted homodetic cyclopeptide as defined in Claim 11, wherein said protected precursor is protected 2-oxyaminoacetic acid (OAA).

13. The method for preparing a grafted homodetic cyclopeptide as defined in Claim 11, wherein said protected masked precursor is a serine residue, the amine and hydroxyl functions of which are protected, and oxidation of which releases an aldehyde group, and preferably is Boc-Ser(tBu)OH.

14. The method for preparing a grafted homodetic cyclopeptide as defined in Claim 11, wherein said protected precursor is a precursor of the thiol function, preferably a dissymmetrical disulfide derivative of cysteine, and very preferably is an Npys group.

15. The method for preparing a grafted homodetic cyclopeptide as defined in any of Claims 11 through 14, wherein firstly substitution of the orthogonal protective groups of the lower face with a label, preferably biotin or fluorescein, is performed; then in a second step the orthogonal protective groups of the upper face of the framework are substituted with a protected precursor of the oxyamine function or of the aldehyde function.

16. The method for preparing a grafted homodetic cyclopeptide as defined in any of Claims 11 through 14, wherein firstly substitution of the orthogonal protective groups of the lower face of the framework with a protected precursor of the oxyamine function is performed; then, in a second step, the orthogonal protective groups of the upper face of the cyclopeptide are substituted with a protected masked precursor of the aldehyde function.

17. The method for preparing a grafted homodetic cyclopeptide as defined in any of Claims 11 through 14, wherein firstly substitution of the orthogonal protective groups of the upper face of the framework with a protected precursor of the oxyamine function is performed; then, in a second step, the orthogonal protective groups of the lower face of the cyclopeptide are substituted with a protected masked precursor of the aldehyde function.

18. The method for preparing a grafted homodetic cyclopeptide as defined in any of Claims 11 through 17, wherein the oxyamine or aldehyde functions generated from the precursors, previously deprotected, are reacted with one or several molecules of interest or with an intermediate molecule carrying an aldehyde or oxyamine function, respectively.

19. The method for preparing a grafted homodetic cyclopeptide as defined in Claim 18, wherein said molecules of interest are identical to or different from one another.

20. The method for preparing a grafted homodetic cyclopeptide as defined in either of Claims 18 or 19, wherein said molecules of interest are nucleic acids, peptides, oligosaccharides, or organic molecules.

21. The method for preparing a grafted homodetic cyclopeptide as defined in Claim 20, wherein at least one of the molecules of interest is the cyclopentapeptide c(RGDfK).

22. The method for preparing a grafted homodetic cyclopeptide as defined in any of Claims 18 through 21, wherein the oxyamine function of the precursor located on the framework is reacted with at least one molecule of interest carrying an aldehyde function, then the precursor of the aldehyde function located on the framework is oxidized and the reaction is continued by bringing the framework into contact with a molecule of interest or an intermediate molecule carrying an oxyamine function.

23. The method for preparing a grafted homodetic cyclopeptide as defined in any of Claims 18 through 22, wherein said intermediate molecule on the one hand carries an oxyamine function capable of reacting with the aldehyde function(s) located on the framework, and on the other hand carries a precursor of at least one aldehyde function.

24. The method for preparing a grafted homodetic cyclopeptide as defined in any of Claims 3 through 23, wherein it is entirely or partially automated on a peptide-synthesizing robot.

25. A grafted homodetic cyclopeptide,
wherein it is obtained by the method as defined in any of Claims 1 through 24.

26. The grafted homodetic cyclopeptide as defined in Claim 25, wherein it is grafted on one of its faces with a ligand of integrin $\alpha v \beta 3$, preferably peptides derived from cyclo(RGDfK) and/or cyclo(RGDyK), which are ligands of integrin, and on the other of its faces with an apoptogenic peptide of the KLAKKLAK type, a known therapeutic organic molecule of the doxorubicin type, or a protein that is toxic at the intracellular level.

27. The grafted homodetic cyclopeptide as defined in Claim 25, wherein it is grafted on one of its faces with a ligand of integrin $\alpha v \beta 3$, preferably peptides derived from cyclo(RGDfK) and/or cyclo(RGDyK), which are ligands of integrin, and on the other of its faces with a detectable molecule of the chromophore, biotin, fluorophore, radioemitter type, or a precursor.

28. The grafted homodetic cyclopeptide as defined in Claim 25, wherein it is grafted on one of its faces with carbohydrate derivatives and on the other face with one or several T-dependent epitopic peptides, one or several cytotoxic peptides, one or several therapeutic organic molecule(s), or a protein that is toxic at the intracellular level.

29. The grafted homodetic cyclopeptide as defined in Claim 25, wherein it is grafted on one of its faces with carbohydrate derivatives and on the other face of the framework with one or several chromophore(s), one or several biotin(s), one or several fluorophore(s), one or several radioemitter(s), or a chemical precursor group or ligand.

30. The grafted homodetic cyclopeptide as defined in Claim 25, wherein it is grafted on one face with B-dependent epitopes of the carbohydrate type, or T-dependent epitopes, and an immunoadjuvant.

31. A therapeutic or diagnostic composition,
wherein it comprises a grafted homodetic cyclopeptide as defined in Claim 25.

32. Use of a cyclopeptide as defined in Claim 25, or a composition as defined in Claim 31, for production of a medication intended to treat cancer.

33. Use of a cyclopeptide as defined in Claim 25, or a composition as defined in Claim 31, for production of a tool for diagnosing cancer.

34. Use of a cyclopeptide as defined in Claim 25, or a composition as defined in Claim 31, for the diagnosis of neoangiogenesis.

35. Use of a cyclopeptide as defined in Claim 25, or a composition as defined in Claim 31, for the suppression of neoangiogenesis.